PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Confirmation No. 9697
	)	
Sallberg *et al.*	)	Group Art Unit: 1648
	)	
Serial No. 09/466,035	)	Examiner: A.M. Wehbé
	)	
Filed: December 17, 1999	)	Atty. Dkt. No. PP001231.0105 (002441.00249)

For: **METHODS OF NUCLEIC ACID IMMUNIZATION**

DECLARATION OF JEFFREY ULMER PH.D. UNDER 37 C.F.R. § 1.132

U.S. Patent and Trademark Office
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

I, Jeffrey Ulmer declare as follows:

1. I am the Global Head for External Research in the Vaccines Research Division at Novartis Vaccines and Diagnostics, Inc. I have a Ph.D. in Biochemistry (McGill University), a Post-Doctoral Fellowship in Cell Biology (Yale University), and ~20 years of experience in the discovery and development of vaccines at Merck Research Laboratories, Chiron Corporation and Novartis (a copy of my cv is attached).

2. I have reviewed the final Office action of September 3, 2008, and the Office action dated May 8, 2009. I have also reviewed Dubensky *et al.* (WO 95/07994; "Dubensky") and Hu *et al.* (AIDS Res. Hum. Retrovir. 7:615-620 (1991); "Hu").

3. As shown in Exhibit 1, experiments were performed by Novartis Vaccines and Diagnostics, Inc. to assess the immune responses to compositions administered according to a prime-boost protocol of the invention. The protocol used is shown on slides 1 and 2. Resistance to viral challenge was assessed in the macaque model, which is art-recognized for use in assessing protection from HIV infection.

4. The results of immunogenicity and efficacy studies with alphavirus replicon vector particles in macaques are shown in Exhibit 1, slide 4, which presents graphs showing viral replication. The best immunogenicity and protection were seen in animals primed with alphavirus and boosted with protein (slides 3 and 4), irrespective of the route of administration of alphavirus. Intranasal and intrarectal administration of alphavirus induced intermediate levels of neutralizing antibodies (slide 3) and protection (groups 1 and 2, slide 4), whereas intramuscular administration (group 3, slide 4) showed strong immunogenicity and protection in every subject animal. In contrast, administration of alphavirus vector during both the prime and boost produced much lower levels of neutralizing antibodies (slide 3) and protection (group 4, slide 4), even though the replication incompetent alphaviral vector was able to express multiple copies of the protein antigen.

5. Exhibit 2 shows that rabbits immunized using an alphavirus prime-protein boost schedule responded with the higher titers of neutralizing antibodies against HIV SF-162,

compared to immunization with protein alone or alphavirus vector alone, demonstrating that the claimed method provides robust immune responses in an additional animal model.

6. Dubensky describes only repeated alphavirus administration. It does not teach a protein boost. Results from the present invention are significantly improved over Dubensky alone (see exhibits 1 and 2). Hu's disclosure is limited to the use of vaccinia, a replicating DNA virus. Hu contains no description or suggestion that its protocol should be applied to a non-replicating RNA vector, such as an alphavirus replicon vector. Hu provides no basis for a skilled artisan to expect the robust responses obtained using the non-replicating alphavirus replicon vector prime and protein boost protocol of this invention.

All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 9/4/09

Jeffrey Ulmer, Ph.D.